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Review

Electromagnetic field and brain development

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ABSTRACT

Rapid advances in technology involve increased exposures to radio-frequency/microwave radiation from mobile phones and other wireless transmitting devices. As cell phones are held close to the head during talking and often stored next to the reproductive organs, studies are mostly focused on the brain. In fact, more research is especially needed to investigate electromagnetic field (EMF)'s effects on the central nervous system (CNS). Several studies clearly demonstrate that EMF emitted by cell phones could affect a range of body systems and functions. Recent work has demonstrated that EMF inhibit the formation and differentiation of neural stem cells during embryonic development and also affect reproductive and neurological health of adults that have undergone prenatal exposure. The aim of this review is to discuss the developing CNS and explain potential impacts of EMF on this system.

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1. Introduction

Because of widespread use of cellular phones all around the world, even at early ages, the effects of EMF emitted by cellular phones on living organisms and human health have recently become one of the most important research topics. Therefore, researchers who keep an ear close to the ground have conducted several scientific studies to examine the health problems that may arise as a result of EMF exposure and to minimize their impacts on humans (Koyu et al., 2005; Manikonda et al., 2007; Balassa et al., 2013; Komaki et al., 2014). Holding cellular phones closely to the ear and headmay result in EMF exposure in the structures

Abbreviations: EMF, electromagnetic field; CNS, central nervous system; BDNF, brain-derived neurotrophic factor; NGF, nerve growth factor; NT-3, neurotrophin 3; NT-4, neurotrophin 4; MRI, magnetic resonance imaging; LP, lipid hydroperoxides; MPO, myeloperoxidase; DNA, deoxyribonucleic acid; H_2O_2, hydrogen peroxide; OH, hydroxyl radical; ROS, reactive oxygen species; RCOO, organic peroxides; IgG, immunoglobulin G; eNSCs, embryonic neural stem cells; GSM, global system for mobile communications; Aβ, amyloid beta; ALS, amyotrophic lateral sclerosis; ELF, extremely low frequency; PD, Parkinson's disease; CAT, catalase; SOD, superoxide dismutase.

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surrounding ears and head. In those individuals, central and peripheral nervous system, which coordinates vital functions, is also affected (Frey, 1998; Odacı et al., 2008; Bas et al., 2009). Numerous experimental and clinical studies have been conducted to investigate the effects of EMF on the central and peripheral nervous system (Odacı et al., 2008; Bas et al., 2009; Chen et al., 2014). Studies using human and animal models yielded significant findings such as increased headache (Frey, 1998; Hocking, 1998), disruption of sleep patterns, and alterations in synaptic plasticity, neurotransmitter release and the life cycle of nerve cells due to cellular phone use (Wagner et al., 1998; Borbély et al., 1999; Manikonda et al., 2007; Maaroufi et al., 2011).

In prenatal and postnatal life, exposure to EMF possibly stimulates neuronal cell death and prevents transformation of stem cells into neurons (Salford et al., 2003). In this point, when we took a brief look at the scientific literature, the effect of EMF exposure on the development of the brain, especially with regard to prenatal development, has not yet been established. Therefore, this review provides general information about brain development process and the effects of EMF on neurodevelopment.

2. What do we know about the electromagnetic field?

EMF is a physical field produced by moving and electrically charged particles and formed by rotation of electrons within the atoms and the core. All entities have an EMF. This field is invisible, imperceptible, but measured by sensitive devices and the results can be determined. The electromagnetic wave is the common name of electromagnetic wave and magnetic field waves spreading in outer space or in a material environment. Cosmic, gamma, x, ultraviolet, visible region, infrared, microwave, and radio waves are all electromagnetic waves and they establish the main operation principle of wireless communication tools which are frequently used in daily life. The high-frequency waves have the greatest energy. At this point, the form of electromagnetic waves affects the properties of EMF (Behari, 1999). Electromagnetic waves have two main effects on tissues namely, thermal effect and

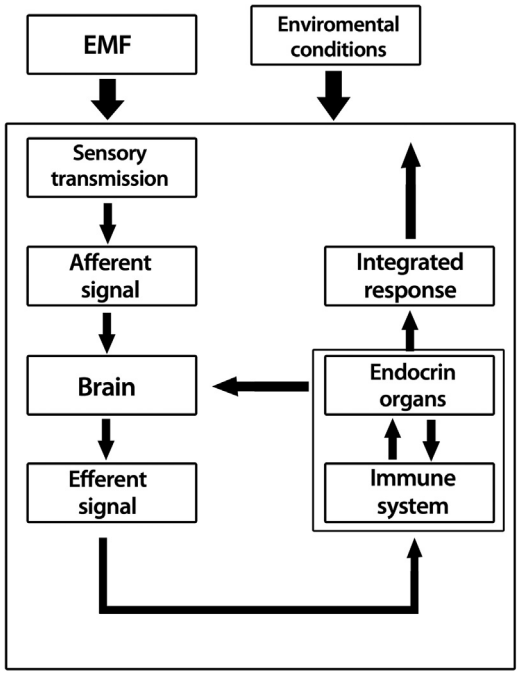

Fig. 1. The proposed control system that mediates EMF-induced biological effects (Modified and redrawn from Carrubba and Marino, 2008).

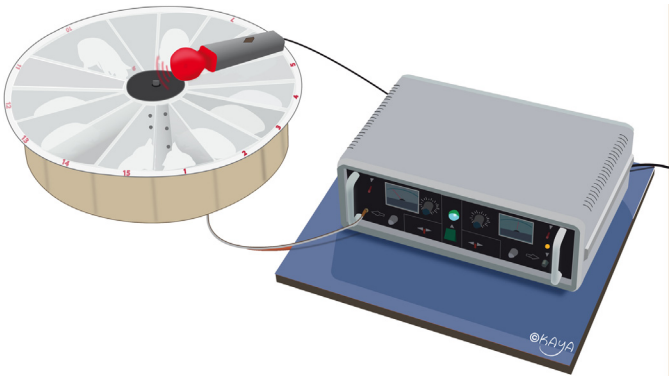

Fig. 2. Micrograph shows the electromagnetic exposure system producing 900 MHz EMF similar to a mobile phone frequency. It shows the application of the EMF exposure to rats in the round plastic EMF cage with a monopole antenna over it.

chemical (non-thermal) effect. While high-frequency electromagnetic waves primarily cause heating-damage (heat-dependent damage), long-term exposure to low frequency electromagnetic waves produce harmful effects in tissues caused by chemical environmental changes (Rothman, 2000) (Fig. 1).

Non-ionizing electromagnetic waves, which occupy a great place in broad-spectrum EMF are, transmitted from several electrical systems such as radars, communication instruments, high-voltage lines, radio and television transmitter, transformer stations and household electrical appliances. Scientific studies conducted so far have shown that even at very low intensity and strength, EMF and waves have several biological effects (Ikehara et al., 1998; Burchard et al., 1999; Aydin and Akar, 2014). Since the amount of EMFs in the natural environment are less than those of created by humans, it is not possible for the living creatures in the world to develop a specific defence mechanism against the potential impact of these areas. There are many studies in the literature on EMF exposure. In these studies, the effects of EMF on body weight, morphology and histology of organs, haematological parameters, biochemical parameters, hormones, immune system and blood electrolyte levels were investigated and different results were obtained (Moustafa et al., 2001; Ozguner et al., 2005; Aydin and Akar, 2014). Of these studies, while some reported that EMF causes adverse effects in the body (Savitz and Loomis, 2005; Komaki et al., 2014), others emphasized their useful and therapeutic effects (Basset, 1993; Galloni et al., 2005, 2009; Valentini et al., 2011). In this point; the application of the EMF exposure is shown in Fig. 2.

Considering all these studies, the diversity of results can be attributed to some reasons. The primary reason is the methodological differences in the studies. Others are variability of the statistical methods used and different criteria followed in the interpretation of the results. Perhaps the most striking one is the diversity of organizations that provide support to the studies (Valentini et al., 2011).

Animal model studies showed that high frequency EMFs may have an influence on the nervous system. In their study, Bas et al. (2009) reported significant pyramidal cell loss in the hippocampus of juvenile rats in the postnatal period, which were exposed to EMF in prenatal period. When the hippocampus of the animals that were exposed to EMF were evaluated histopathologically, some changes such as darkening of pericarion of pyramidal cells, downsizing and deterioration in pericarions were observed in experimental group in comparison to the control group.

Additionally; in Odacı et al. (2008)'s study, the effect of EMF on dentate gyrus in rats exposed to 900 MHz EMF in the prenatal period was investigated histologically. When the results were analyzed, it was observed that prenatal exposure to EMF causes substantial loss of granule cells during the postnatal life (Fig. 3).

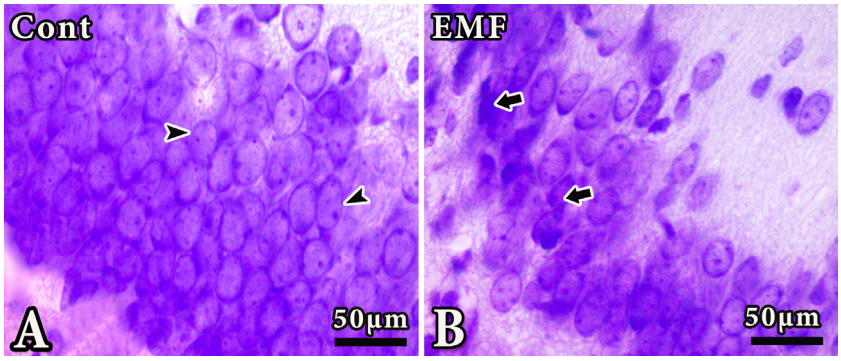

Fig. 3. The photomicrographs of the dentate gyrus in the control (A) and EMF (B) groups are seen. Despite of the intact shape of granular cells of dentate gyrus in the control, some of the granular cells in the related area of the EMF group were condensed. Arrows (B) point to condensed cells and arrowheads (A) show the healthy granular cells (Cresyl violet staining: Scale bars: ×100 magnification). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Inhibition of neurogenesis can be considered as one of the reasons responsible for reduction in the number of granule cells caused by prenatal exposure to EMF. The effects of EMF emitted by cellular phones on living organisms and human health have become an important research topic for several reasons. The most important one is that cellular phones and cellular phone-related technology yields significant economic benefits. Because its economic return is quite huge, large companies operating in the international dimension may sometimes manipulate these studies. Therefore, in order to obtain relevant results, powerful statistical methods using appropriate techniques and detailed experimental study design should be used and blind studies should be preferred (Valentini et al., 2011).

It is inevitable to expose to the EMF emitted by cellular phones, which are one of the indispensable tools of our daily lives. Despite diversities in the results of the studies, the effect of EMFs on living organisms is a well-known fact. There are studies indicating the adverse effect of EMFs on prenatal and postnatal development and different functions of organisms. At this point, further studies are needed to expose the biological effects of EMF on the body and human health and to determine that whether it causes permanent damage.

3. Brain development

3.1. Origin of the nervous system

Development of the neuronal system is highly complex and long process, and similarly brain development is a part of this process as well has more complex molecular mechanisms and hormonal changes independently of this process. The CNS develops from a flat mass of tissue called the neural plate. Notochord and paraxial mesoderm stimulate ectoderm to differentiate into neural plate. Neural folds, neural tube and neural crest develop from neural plate. Neural tube is differentiated into CNS (Moore et al., 2013). Neural plate and neural tube formation, a process known as neurulation, starts at the beginning of the 4th week (22nd–23rd days). The walls of the neural tube thicken to form the brain and the spinal cord. Neural canal forms ventricular system of the brain and canalis centralis of medulla spinalis (Stiles and Jernigan, 2010; Moore et al., 2013). Some mesenchymal cells migrate from primitive node and pit to the cranial and createa cellular cord called notochord extension in the centerline. A lumen creates a notochord channel in this extension in a short time. Notochord extension reaches prechordal plate, a small, cylindrical area consisting of endodermal cells, located between the ectoderm and endoderm.

Rod-shaped hollow notochord extensions can no longer move forward, because it is tightly attached to the ectoderm, which is located onto the prechordal plate. Vertebral column extending from oropharyngeal membrane to primitive node is formed around the notochord. As the neurocentrum is created, notochord degenerates and disappears; only continues its existence in nucleus pulposus of each intervertebral disc and stimulates thickening of embryonic ectoderm and formation of the neural plate, primordium of CNS (Moore et al., 2013).

3.2. Neurulation (formation of neural tube)

Development of notochord induces thickening of the ectoderm and ultimately result in formation of structure known as neural plate, which is composed of long neuroepithelial cells. The CNS develops from ectoderm of neural plate. As the notochord lengthens, neural plate expands and moves toward cranial oropharyangeal membranes. At about 18th day, neural plate is invaginated along with the central axis and forms neural groove which extends longitudinally in the center line. Neural folds on the cranial end of the embryo are fluffy, the first sign of brain development. At the end of the third week, the neural folds begin to close up merge. Neural plate changes into neural tube and this

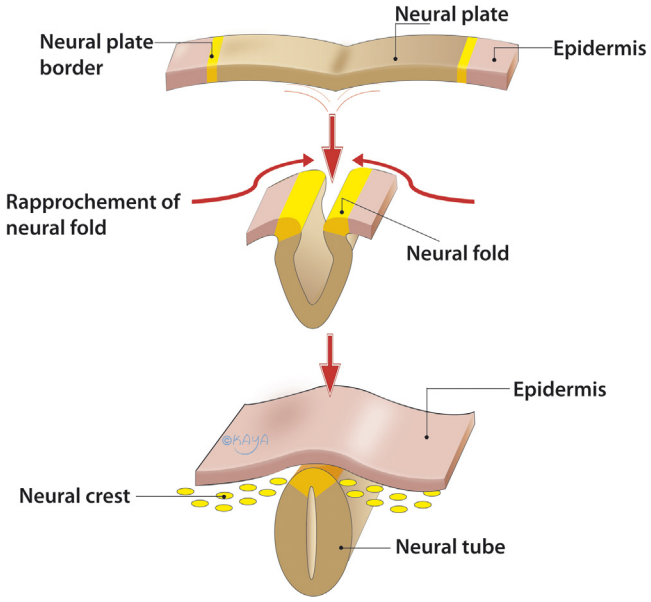

Fig. 4. Formation of neural tube and neural crest (Modified from Moore et al., 2013).

formation is completed in the fourth week of neurulation (Stiles and Jernigan, 2010; Moore et al., 2013) (Fig. 4).

As the neural folds coalesce to form neural tube, some neuroectodermal cells extending along the edge of each fold lose their connections with epithelium and neighbouring cells. When the neural tube is separated from surface ectoderm (external ectoderm), neural crest cells migrate to the both sides of the neural tube dorsolaterally. These cells then form the neural crest, which extends over the neural tube and surface ectoderm (Stiles and Jernigan, 2010; Moore et al., 2013). Neural crest cells are differentiated into several cell types such as spinal ganglion and autonomic nervous system ganglion. These cells also form peripheral nerve sheath and covers of the brain and the spinal cord (Lenroot and Giedd, 2006; Moore et al., 2013).

The brain develops from neural tube in the cranial of 4th pair of somites. Before complete joining of neural folds, three different vesicles appear in the rostral end of the neural tube. From rostral to caudal, these primary brain vesicles are forebrain (prosencephalon), midbrain (mesencephalon) and hindbrain (rhombencephalon). Then, the forebrain is divided into two secondary brain-vesicles as telencephalon and diencephalon at the beginning of the third week. Hindbrain is divided into two main sections as metencephalon and myelencephalon at the 5th week (Stiles and Jernigan, 2010; Moore et al., 2013).

3.3. *Neurotrophic factors*

Neurotrophins including brain-derived neurotrophic factor (BDNF), Nerve growth factor (NGF), neurotrophin 3 (NT-3) and neurotrophin 4 (NT-4) have emerged recently as potent intracellular factors for neuronal plasticity. Neurotrophins play a crucial role in programed cell death (apoptosis) in the CNS). When they decrease in number due to various internal and external reasons, biological sequence of events, which result in neuron death in the brain, is triggered (Tongiorgi, 2008).

Human brain maturation is a complex, lifelong process. Reproduction, maturation and migration of cells in the cortex and subcortical gray matter during fetal period are a careful and sequential process. There are about 100 billion neurons in the human brain at birth. Newborn brain is nearly one third or fourth of adult brain. The brain that is positively or negatively modified by environmental factors continues to develop based on genetic program. Today, detailed examination of the human brain is possible through imaging methods. In children aged 5–11 and followed for two years via Magnetic Resonance Imaging (MRI), brain development was shown to be 1 mm per year especially in the prefrontal cortex (Sowell et al., 2004; Stiles and Jernigan, 2010). Maximum total cerebral volume is reached in early adolescence (Giedd et al., 1996). The brain develops and changes significantly during adolescence. Reconstruction of neural networks, changes in some brain regions, increase in the amount of white matter and reduction in the amount of gray matter has been reported during this period (Benes, 2003; Blumberg et al., 2003). MRI studies showed increased gray matter just before the onset of puberty but reduction afterwards (Giedd, 2004; Lenroot and Giedd, 2006). At cellular level, the reason for this change is the overproduction of axons and synapses in early adolescence and the rapid synaptic pruning after puberty (Andersen and Teicher, 2004; Stiles and Jernigan, 2010).

The increase in gray matter continues till the early and middle adolescence and then decreases with a ratio of 5% decennially (Giedd et al., 1999; Courchesne et al., 2003). Specifically, in cross-sectional analyses, gender differences are also significant. Both the cerebellum and the brain are significantly larger (by 7–10%) in boys

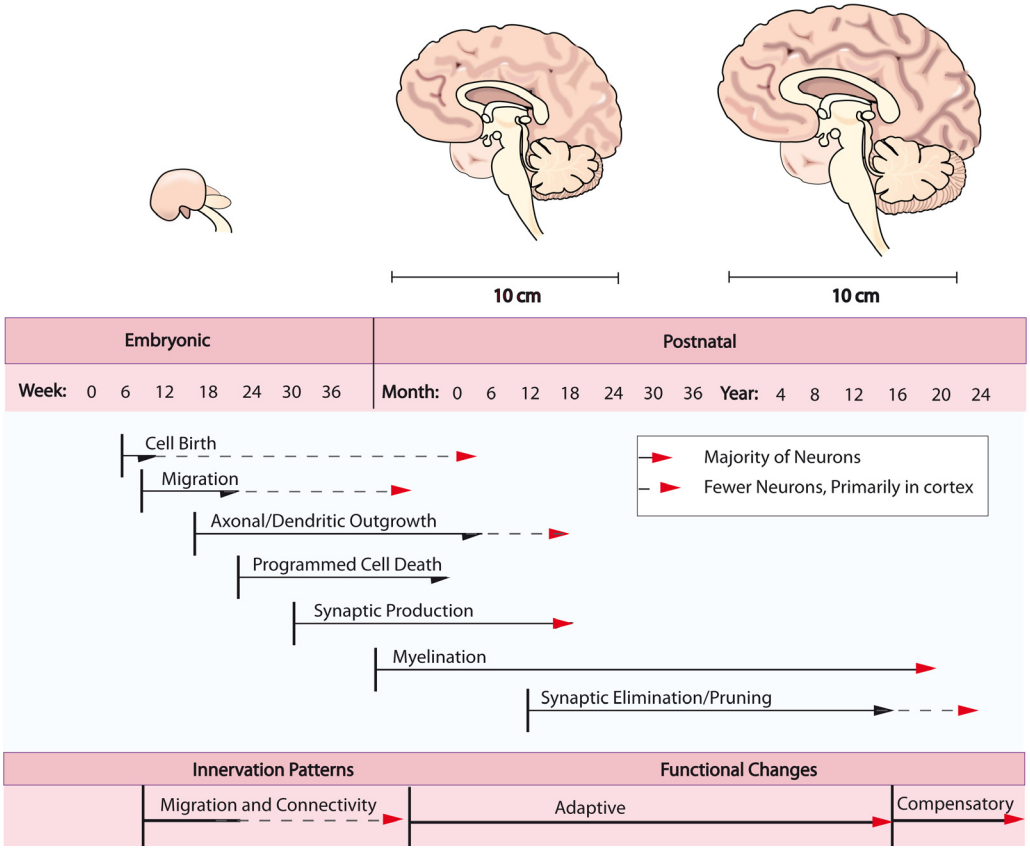

Fig. 5. The stages of brain development (top) and different windows of vulnerability (bottom). (Redrawn from Andersen, 2003).

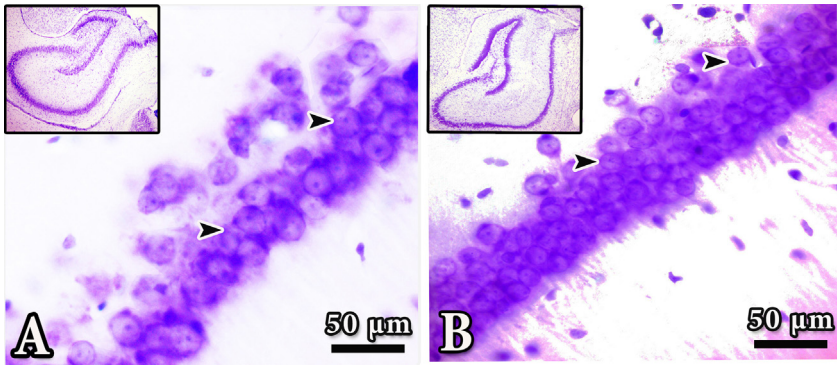

Fig. 6. Histological section of pyramidal cells from 1 week hippocampus indicating the site of (A) and 8 week adult rat hippocampus indicating the site of (B). Arrowheads indicate the structure of the pyramidal neurons (Cresyl violet staining: Scale bars: ×40 magnification). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

than girls. Concordantly, cortical gray matter is 10% larger in boys than girls. On the other hand, left and right volumes of caudate and left globus pallidus are greater in girls than boys (Krain and Castellanos, 2006). In addition, hippocampal volume in girls and the amygdala volume in boys are greater (Fig. 5).

This difference in hippocampal and amygdala volume may be associated with attention deficit, hyperactivity and Tourette's syndrome (disorder) and neuropsychiatric disorders such as early-onset obsessive-compulsive disorder (Aylward et al., 1996; Castellanos et al., 2003; Peterson et al., 2003).

In conclusion, all other important regions of the brain (hippocampus, amygdala, nucleus accumbens, prefrontal, frontal, orbital cortex and the limbic system) are restructured during adolescence (Fig. 6).

Especially, the volume of prefrontal cortex in humans and animals reduces throughout the adolescence (Sowell et al., 1999, 2001; Stiles and Jernigan, 2010). Development in some regions of the brain continues till the second and third decades of life. While the volume of the brain reduces in late adolescence and early adulthood, it remains constant in mid-adolescence. This volume loss is due to several biological factors such as maturation of synapses and brain cells. While the changes in synapses are associated with pruning, the changes in the brain cells are associated with mutation, stratification and apoptosis (Giedd et al., 1999; Kennedy et al., 2002).

4. Effects of electromagnetic field on brain development

Several studies on the EMF, it was occurs oxidative stress and reactive oxygen species that is caused loss of cells and blocked their production. Additionally, EMF is decreasing the antioxidant enzymes capacities it was detected. The oxidative stress parameters, which are, increased lipid hydroperoxides (LP) and myeloperoxidase (MPO) activity in immature rats. This is indicator the immature rats more exclusive than the mature rats for EMF exposure. The EMF exposure classified class 2B carcinogen by the expert scientists (Hankin, 2003).

The human brain development is continues in third gestational week. The neural progenitor cells play a major role, which are molecular and cellular differentiation through adolescence. The stage of development is easily affected to physical and environmental factors (Odacı et al., 2015). Beginning the embryonic day 42, the neuron production starts in the human brain.

Brain development continues prenatal term process that begins and until puberty. It was reported that EMF exposure was associated with neurological diseases such as Alzheimer's disease that is increasing the level of amyloid beta, a risk factor, in the brain. Long-term EMF exposure may result in Alzheimer disease like symptoms due to enhancing oxidative stress (Jiang et al., 2013). Contrarily, several studies focused on cognitive benefit of EMF exposure. Especially, a study of Arendash et al. (2012), on the Alzheimer models of old transgenic mice, has claimed a cognitive benefit of long-term EMF exposure (Arendash et al., 2012). Arendash et al. (2010) also reported protective effects of long-term EMF exposure on cognitive activity and Aβ neuropathology of transgenic mice against Alzheimer disease. EMF-induced therapeutic approaches are to enhance the brain mitochondrial dysfunction and accordingly cognitive benefit on brain regions such as cerebral cortex and hippocampus occurs in Alzheimer disease (Arendash et al., 2010).

Epidemiological studies as well as experimental studies on effects of mobile phones or GSM modulated electromagnetic field were examined. These studies have shown that EMF may also have beneficial effects on cognitive activity, for this reason it is suggested that it may be used for treatment of some CNS disorders. On the other hands, after heavily using of mobile phone, headache and vertigo more often were reported. Also some epidemiological data revealed that rate of migraine may increase after long-term use of cellular phones (Arns et al., 2007). The adverse effects of GSM modulated EMF such as oxidative stress reveal by changing the calcium levels in neurons. This is especially found in negative effects on brain development is highly sensitive to EMF exposure in the prenatal period (Hardell and Sage, 2007).

The free radicals occur in cells with the EMF exposure. This is damages the structure of the cell vital components such as proteins, membrane and deoxyribonucleic acid (DNA), and causes the formation of carcinogenesis. In studies on EMF is stated that the increase of free radicals in cells by Fenton reaction. This processes results in hydrogen peroxide (H_2O_2), hydroxyl radical (OH) is formed. Hydroxyl radical is the strongest reactive oxygen species (ROS). Where the resulting thiols and various molecules such as fatty acids a proton breaking thiyl radicals, organic carbon-centered radicals, organic peroxides (RCOO) as the formation of new toxic radicals and ultimately causes major damage (Lai and Singh, 2004; Hardell and Sage, 2007). At the end of the free radicals, with a greater number of disulfide bond in the structure immunoglobulin G (IgG), and disrupted tertiary structure of proteins such as albumin, carries out their normal functions (Fig. 7).

OH readily reacts with deoxyribose and base and lead to changes. Hydrogen peroxide from neutrophils constitutively activated and cell membranes easily reached through the core to DNA damage, cell dysfunction and even cause cell death. In the first two weeks of embryonic life is the cell in the form of most stem cells, and these cells are very sensitive to toxic effects.

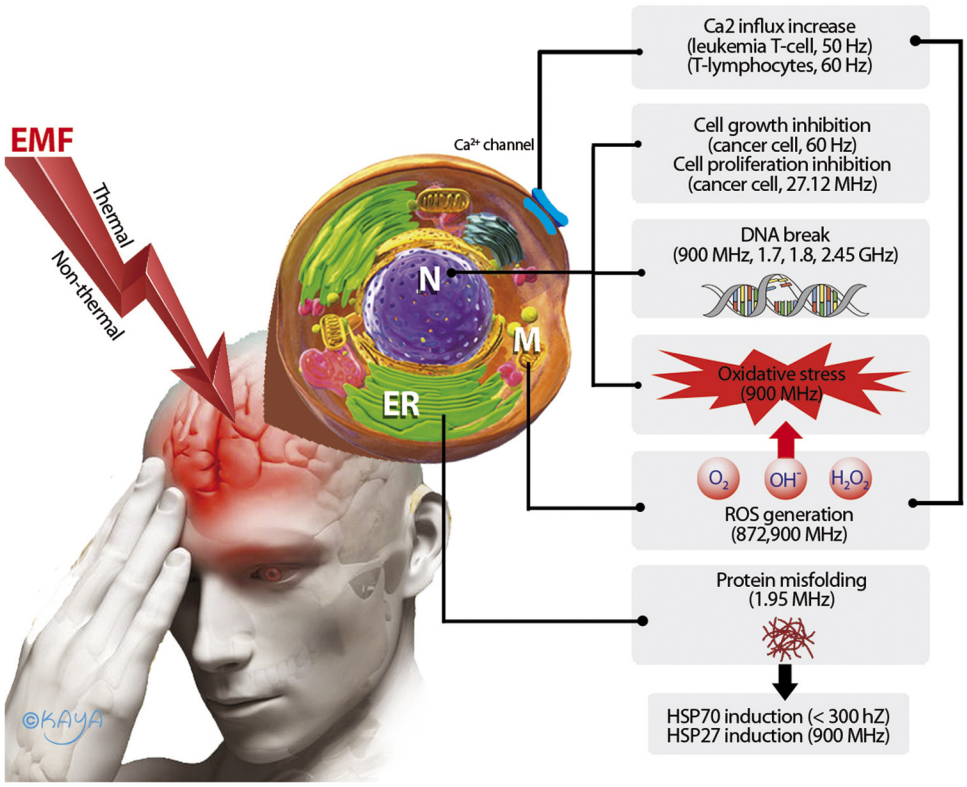

Fig. 7. The effect of EMF in the brain is illustrated at the cellular level. N: Nucleus, ER: endoplasmic reticulum, M: Mitochondria. (Redrawn from Gye and Park, 2012).

Embryonic exposure to toxic effects in this way can lead to increased risk of growth retardation and birth defects (Leeka et al., 2005).

Recent studies suggest that some parts of CNS continued throughout the life of the neuron production. Connections between synapses in the human brain make about 2 years old peak and which are lost unnecessarily in adulthood (Rodier, 2004; Leeka et al., 2005). This stage the brain after the birth in terms of the new synapse formation, excess synapse formation between neurons and elimination of redundant connection it is important. Which is the myelination of neurological events that occur after birth is insufficient information about the extent to which environmental and toxic affect the child affected (Rodier, 2004). Brain cancers seen with in children, embryonic or mesodermal origin, and they are especially brain stem gliomas. The adult tumours occur in the epithelial tissues especially to cerebral hemisphere.

Studies in recent years have shown that the EMF is increase of the incidence of brain cancer, furthermore highly affected cognitive function and cause the decreased number of neuron in the hippocampus on children CNS (Merzenich et al., 2008; Abramson et al., 2009; Thomas et al., 2010; Söderqvist et al., 2011).

As well known, fetuses and infants have a large amount of stem cells. Embryonic neural stem cells (eNSCs) have a critical role in fetal brain development because they are responsible for the formation of the fetal nervous system (Franco et al., 2012). This proliferation of stem cells, some of the most important steps which are neuronal and glial cell differentiation, cell death, and the development of the neuritis. And differentiation into various cell such as astrocytes and oligodendrocyte cells, are the most sensitive to EMF exposure (Davis and Lowell, 2008; Buzanska et al., 2009). In studies conducted on this topic reported that changes in transcript levels of apoptosis related genes in embryonic stem cell-derived neurons were observed (Nikolova et al., 2005). Besides, as a result of in utero exposure 900 MHz EMF was determined in rat brain neuronal loss (Bas et al., 2009).

Czyz et al. (2004) indicated that Global System for Mobile Communications (GSM) cell phone exposure affected gene expression levels in embryonic stem cells (p53-deficient); and significantly increased heat shock protein HSP 70 production.

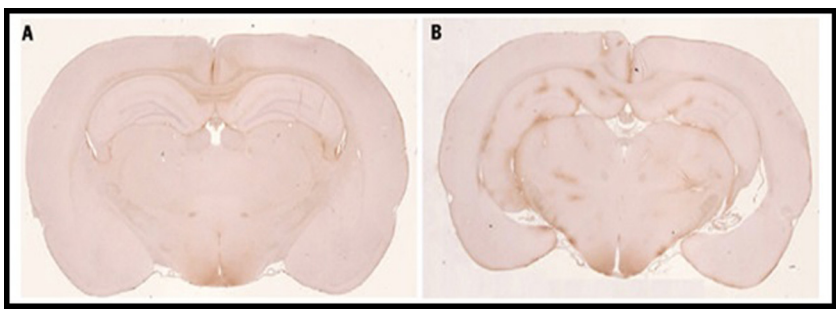

Fig. 8. The figure shown that brain samples of a sham-exposed control animal (A), and animal exposed to 2 mW/kg for 2 h (B). In albumin there was a normal feature in the hypothalamus.

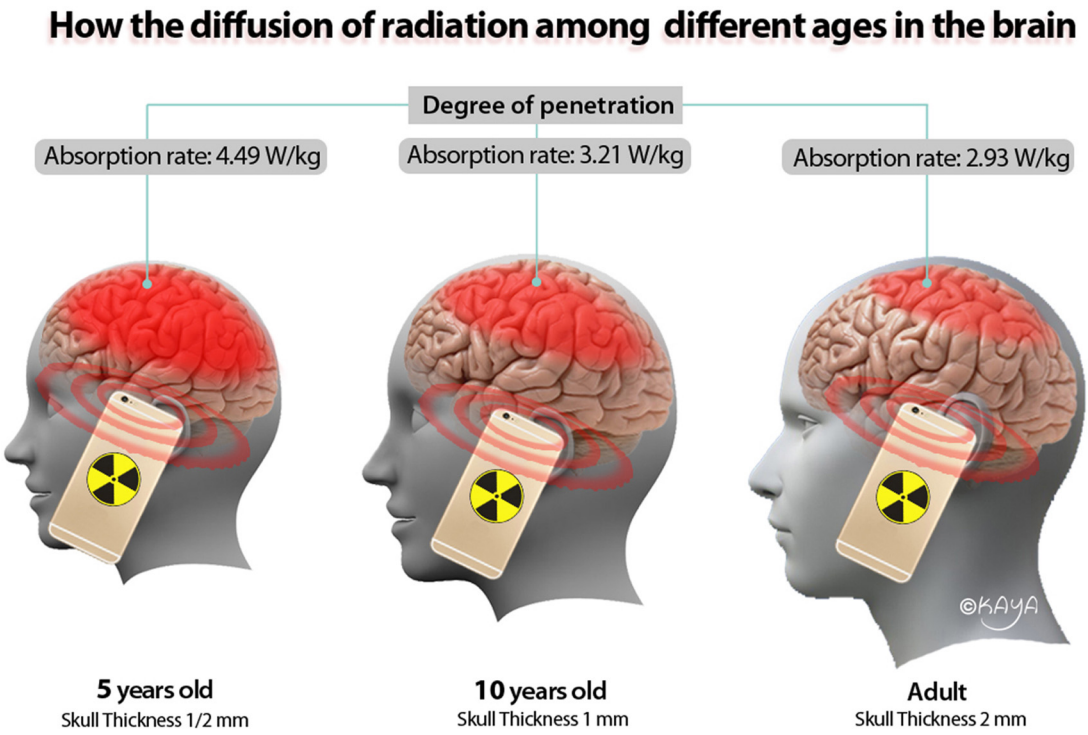

Fig. 9. EMF is a deeper penetration into the brain of children and young people. And children absorb more energy than adults from the same phone. Furthermore, children's immune system is not as well developed as adults (Redrawn from Gandhi et al., 1996).

Another researcher reported that 915 MHz electromagnetic wave exposure negative effects in human stem cells and it might be caused cancer (Belyaev et al., 2010). In recent animal experiments, the embryos of pregnant mothers' exposure to EMF hyperactivity have been observed to cause cognitive and memory impairment in the offspring (Aldad et al., 2012).

A histological study, exposed to 900 MHz EMFs during the prenatal period of 4 weeks in rat hippocampus were counted by unbiased stereological counting methods, it was found to be a significant reduction in the number of pyramidal neurons (Bas et al., 2009). As well as, the reported that 900 MHz EMF's is changed brain blood barrier permeability (Salford et al., 2003; Nittby et al., 2009, Fig. 8). And the other in vitro study investigated that 1.8 GHz EMF is caused increase permeability blood brain barrier to sucrose (Schirmacher et al., 2000). There was an albumin a lot of small foci leakage from the various vessels after the EMF exposure (Salford et al., 2003).

All these studies, as well as 50 Hz EMF increases neuronal differentiation of neural stem cells and replacement applications of stem cells (Morgado-Valle et al., 1998; Piacentini et al., 2008), which is a non-chemical method promotes neuronal differentiation (Cho et al., 2012). The authors found that mice exposed to extremely low-frequency electromagnetic fields (ELFEFs) showed increased hippocampal neurogenesis. They also explained this effect by molecular biology that the gene expression in hippocampal neural stem cells has announced as the fulfilment of pro neuronal differentiation (Leone et al., 2014). Also, Puromycin and H_2O_2 apoptosis induced by are inhibited by the 50 Hz EMF and has been reported to enhance the proliferation (Grassi et al., 2004).

Young children and skull thickness is very thin. Therefore, EMF absorption rate is higher in children and adolescents compared to the adults (Fig. 9). The radiation penetrates the skull of adult (25%), young (50%) and a 5 year old (75%).

4.1. Electromagnetic field is related with the several neurodegenerative disorders

Several studies have indicated that EMF is led to the emergence of reactive oxygen species in the cell. There are many neurodegenerative diseases, which are associated with the ROS resulting in brain cells. Alzheimer's disease is characterized by loss of neurons in the cerebral cortex and hippocampus. The pathogenesis of the disease started amyloid plaques; accumulate in the spaces between nerves cells are caused by the death of nerve cells. Cells occurring ROS are the leading causes of redox-generated hydroxyl radicals, and can promote the synthesis of amyloid beta (Aβ) protein precursor in an oxidative stress-mediated pathway. In this regard EMF increases the levels of ROS in the cells may increase the risk of Alzheimer's disease. As well as EMF, many environmental factor, (exposures to aluminum, solvents, and pesticides) and physiological factor (age, family history of dementia, and Apo lipoprotein E ε4 genotype) is effective in the pathogenesis of the Alzheimer disease. However, it was reported that short and repeated pulsed of EMF would be used in the reduction of ROS production in the cellular defence mechanism. According to these studies, a prolonged electromagnetic therapy results in lower mitochondrial activity and proliferation rate. In the oxidative pathways, an increase of heat shock protein HSP70 and the free radical scavenger superoxide dismutase-1 enzyme (SOD-1) was observed. It was studied on effects of 50 Hz power line frequency magnetic field on the CNS by EEG analysis. According to the measuring of nerve conduction velocity and heart rate variability, no significant effect on the nervous system in rats following exposure of 2 min 50 Hz, 0.3 mT 50 Hz power line frequency magnetic field was observed.

Epidemiological studies have reported a positive effect of 50/60-Hz power transmission fields on leukaemia or lymphoma development. As a result of oxidative stress induced by EMF,

neurodegenerative diseases occur. Furthermore it was reported that exposure to ELF-EMF can change cerebral blood flow of aged Alzheimer disease in the transgenic mice. Reale et al. (2014) was evaluated the effects of 50-Hz EMF on human SH-SY5Y cells as a neuronal cell model. They observed that H_2O_2-induced stress in cells exposed to continuous ELF-EMF results in a decrease in the catalase (CAT) activity and an increase in O_2 levels. According to Falone et al. (2007), continuous ELF-EMF exposure leads to reduction in cell tolerance against oxidative stress.

Del Vecchio et al. (2009) investigated the effects of prolonged exposure to 900 MHz GSM modulated EMF on viability and vulnerability of neuronal cell cultures. They studied on primary cortical neurons and SN56 cell line exposed to 25-35AA beta-amyloid. Slight effects of GSM modulated radiation on SN56 cell vulnerability to oxidative stress was found. Contrarily no statically effect of it on glutamate and beta-amyloid-dependent cell death was observed.

Parkinson's disease (PD) is resulting in the loss of dopaminergic neurons in the substantia nigra. This condition, known as Lewy bodies intra-cytoplasmic neuronal inclusions of α-synuclein which is characterized by the accumulation and neuronal loss is one of the most common neurodegenerative diseases. The oxidative stress is increased the α-synuclein mutation. This pathogenic factor in PD associated with the exposure to EMFs. But, long-term radio frequency stimulation provides cognitive benefits to Alzheimer's disease animals. In a study describing this judgment used highly (80%) neuron-enriched mixed cortical cell cultures from the brains of rat embryos to study the effect of chronic exposure to GSM-900 MHz, at a low SAR (0.25 W/kg) demonstrated that EMFs mediated down regulation of the α-synuclein (Terro et al., 2012).

Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disorder characterized by progressive degeneration of motor neurons in the spinal cord, motor cortex, and brainstem. The first hypothesis has been suggested that exposure to Extremely low frequency (ELF)-EMFs was linked to ALS in 1964 (Haynal and Regli, 1964). However, this issue is a controversial issue, some epidemiological studies have positively correlated ALS death with exposure to EMFs, although a few studies have no report that any connection between the EMF and ALS. So, further studies are needed.

The other neurodegenerative disease is Huntington's disease, which is autosomal dominant. 3NP toxin that is associated with Huntington's disease, triggers energy impairment, cytotoxicity, oxidative stress, and neuronal death. In addition to this, some studies have observed the neuroprotective effects of ELF-EMFs. The ELF-EMFs (60 Hz and 0.7 mT) group was applied along 21 day. If compared to control 3NP-treated animals, ELF-EMFs improved neurological scores, improved neurotropic factor levels, and decreased both oxidative damage and neuronal loss. Furthermore, exposure to EMF prevented loss of neurons in rat striatum. Magnetic stimulation in rats prompts an increase in neuron survival and/or in neuronal density (Tunez et al., 2006; Tasset et al., 2012).

5. Conclusion

In the light of results described here, the effects of species of EMFs on cell biology, apoptosis and neuronal loss are unclear. Given the wide use of mobile communications in everyday life, whether RF-EMF exposure affects brain development is a major concern. The fetus and children brain are more sensitive the electromagnetic exposure. The brain is very sensitive to external factors during this period. Referring to the studies, the cells were observed to be many adverse effects, depending on the severity and duration of the applied EMF. ELF-EMF neuro-degenerative disease was observed on some neuroprotective effects, it is stated that the 900 MHz EMF caused damage in neurons.

In this respect, made it in a variety of electromagnetic frequencies, various immunochemical, biochemical and stereological studies are needed. With advanced technology in everyday life to stay away from the EMF, is almost impossible. Therefore, particular care must be taken when using the power tool. An alternative way to reduce the negative effects of addition may benefit from antioxidant therapy.

Ethical statement

Conflict of interest statement

The authors have no conflict of interest to declare. The authors alone are responsible for the content and writing of this review.

Submission declaration

The present review has not been published previously and it is not under consideration for publication elsewhere, its publication is approved by all authors.

Contributors

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